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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,729	11/17/2003	Jean-Pierre Sommadossi	06171.105062	5135

20786 7590 05/30/2008

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
05/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,729	SOMMADOSSI ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,34,38-40,87,89,92,101 and 103-107* is/are pending in the application.

4a) Of the above claim(s) *38 and 87* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,34,39,40,89,92,101 and 103-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 05 February 2008.

Claims 1-32, 35-37, 41-86, 88, 90, 91, 93-100, 102 and 108 have been cancelled.

Claims 33, 34, 38-40, 87, 89, 92, 101 and 103-107 are pending. Claims 38 and 87 are withdrawn as they don't read on the elected species of 3-L-valinyl-β-D-2'-methyl-cytidine.

Claims 33, 34, 39, 40, 89, 92, 101 and 103-107 are currently examined.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The nonstatutory double patenting rejection of claims 33, 34, 37, 39, 40, 48-50, 89, 100 and 105 as being unpatentable over claim 4 of US Patent No. 7,192,936 B2 is **withdrawn** in response to Applicants' amendment.

The nonstatutory double patenting rejection of claims 33, 34, 37, 39, 40, 48-50, 89, 100 and 105 as being unpatentable over claims 15 and 18 of US Patent No. 7,169,766 B2 is **withdrawn** in response to Applicants' amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 33, 34, 39, 40, 89, 92, 101 and 103-107 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in consideration of Applicant's arguments.

The rejection of claims 33, 34, 39, 40, 89, 92, 101 and 103-107 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in consideration of Applicant's arguments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. §102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. §102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. §102(e)).

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 33, 34, 92, 104 and 107 under 35 U.S.C. §102(e) as being anticipated by Carroll *et al.* (US 7,105,499 B2, priority filing date 22 January 2001, hereinafter "Carroll") is maintained.

The instant claims are directed to a method for treating a HCV infection in a host comprising administering a 2'-branched pyrimidine or its pharmaceutically acceptable prodrug or salt to the host, optionally in combination and/or alternation with one or more drugs that directly or indirectly induce a mutation in a HCV at a location other than a mutation of a nucleotide that results in a change from serine of domain of the RNA polymerase region (NS5B).

Carroll teaches a method of treating RNA-dependent RNA viral infection or Flaviviridae viral infection, more specifically, an HCV infection, by administering a compound like 2'-methyl-cytidine (column 15, line 14-67), in combination or alternation with other agents like ribavirin, viramidine, levovirin, thymosin alpha-1, HCV NS3 serine

protease inhibitor, interferon-a-2b (column 32), VX-497, mycophenolate mofetil, amantadine and 2'-C-branched ribonucleosides (column 33). Thus, the instant invention is anticipated by Carroll *et al.*

Response to Arguments

Applicant's arguments filed 25 February 2008 have been fully considered but they are not persuasive. Applicants argue that Carroll does not teach that the secondary agents listed in column 32 and 33 possess the property of inducing the specified mutations in a HCV.

Firstly, the limitation "in combination and/or alternation with one or more drugs that directly or indirectly induce a mutation in a HCV at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT, of domain B of the RNA polymerase region" follows the word "optionally" in the claim language, thus this limitation is not necessarily considered part of the claimed invention.

Secondly, Applicants already admitted on the record (page 8 of the remark filed on 25 February 2008) that type 1 interferon and HCV protease inhibitors are drug well-known in the art that induce mutations at a location other than serine in HCV NS5B. Carroll specifically teaches interferon α (which is a type 1 interferon) and HCV NS3 protease inhibitors (see column 32) and hence anticipates the instant invention.

Even though Carroll does not expressly teach the claimed functional characteristic of inducing non-NS5B-serine mutations, Carroll discloses the same drug

compounds as claimed in the invention. The mutational property of the interferon α (which is a type 1 interferon) and HCV NS3 protease inhibitors is a new advantageous property of a prior art process disclosed in Carroll. Newly discovered property of prior art cannot support patent on that same art. See MPEP §2112 [R-3]. *Abbott Laboratories v. Baxter Pharmaceutical Products Inc.* 80 USPQ2d 1860, U.S. Court of Appeals Federal Circuit Nos. 06-1021, -1022, -1034. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1251, 1254, 195 USPQ 430, 433 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 39, 40, 89, 101, 103, 105 and 106 under 35 U.S.C. §103(a) as being obvious over Carroll et al. (US 7,105,499 B2, hereinafter "Carroll") in view of Sinko *et al.* (1998, hereinafter "Sinko") is maintained.

The instant invention is further limited to a valinyl ester prodrug of the 2'-branched pyrimidine.

The relevance of Carroll is set forth above. The Carroll patent does not disclose an amino acid ester prodrug.

Sinko discloses valacyclovir (VACV), the L-valyl ester of the acyclic nucleoside analog of deoxyguanosine. Sinko *et al.* further disclose that the mean absolute oral bioavailability of VACV is three to five times that of acyclovir in humans. See page 209, right column, 2nd ¶.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Carroll method so as to replace the 3'-OH group of 2'-branched nucleoside with a valine ester group to make a valinyl ester prodrug with a reasonable expectation of success because Sinko teaches that a valinyl ester prodrug can enhance the oral bioavailability of the nucleoside drug and improve the intestinal uptake of nucleoside analog acyclovir. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 25 February 2008 have been fully considered but they are not persuasive. Applicants argue that Examiner has not cited the Sinko reference on the Office Action form 892. However, a copy of the Sinko reference was included in the Office Action mailed on 16 August 2007. A new Examiner's Notice of References Cited (form 892), containing the citation of the Sinko reference, is hereby attached to the instant Office Action.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Wang whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648